EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

ESRF

Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF.

Once completed, the report should be submitted electronically to the User Office using the **Electronic Report Submission Application:**

http://193.49.43.2:8080/smis/servlet/UserUtils?start

Reports supporting requests for additional beam time

Reports can now be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.

ESRF	**Experiment title:** Solution structure of the SCR-6/-7-8 domains in a fragment of complement factor H	**Experiment number**: SC-2024
Beamline: ID02	**Date of experiment**: 12 Dec 2005 (1 day)	**Date of report**: 28th Feb 2007
Shifts: 6	**Local contact(s)**: Dr Stephanie Finet	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Fernando, A.*, Furtado, P. B.*, Gilbert, H. E.* & Perkins, S. J.* (UCL)

Clark, S. J., Day, A. J., Sim, R. B. (Oxford University)

Report:

Associative and structural properties of the region of complement Factor H encompassing the Tyr402His disease-related polymorphism and its interactions with heparin. (2007) *J. Mol. Biol.* In press. Fernando, A. N., Furtado, P. B., Clark, S. J., Gilbert, H. E., Day, A. J., Sim, R. B. & Perkins, S. J.

Abstract: Factor H (FH) is a major complement control protein in serum. The seventh short complement regulator (SCR-7) domain of the 20 in FH is associated with age-related macular degeneration through a Tyr402His polymorphism. The recombinant SCR-6/8 domains containing either His402 or Tyr402 and their complexes with a heparin decasaccharide were studied by analytical ultracentrifugation and X-ray scattering. The sedimentation coefficient is concentration dependent, giving a value of 2.0 S at zero concentration and a frictional ratio f/f_o of 1.2 for both allotypes. The His402 allotype showed a slightly greater self-association than the Tyr402 allotype, and small amounts of dimeric SCR-6/8 were found for both allotypes in 50 mM, 137 mM and 250 mM NaCl buffers. Sedimentation equilibrium data were interpreted in terms of a monomer-dimer equilibrium with a dissociation constant of 40 μM for the His402 form. The Guinier radius of gyration R_G of 3.1-3.3 nm and the R_G/R_O ratio of 2.0-2.1 showed that SCR-6/8 is relatively extended in solution. The distance distribution function *P(r)* showed a maximum dimension of 10 nm which is less than the length

expected for a linear domain arrangement. The constrained scattering and sedimentation modelling of FH SCR-6/8 showed that bent SCR arrangements fit the data better than linear arrangements. Previously-identified heparin-binding residues were exposed on the outside curvature of this bent domain structure. Heparin caused the formation of a more linear structure, possibly by binding to residues in the linker. It was concluded that the His402 allotype may self-associate more readily than the Tyr402 allotype, SCR-6/8 is partly responsible for the folded-back structure of intact FH, and SCR-6/8 changes conformation upon heparin binding.